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Ductal spasm during percutaneous device occlusion of the patent ductus arteriosus; nightmare of the cath-lab: "winking ductus"

Spasm of patent ductus arteriosus

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Abstract

Aim: The occurrence of intermittent spasms and subsequent patency of the patent ductus arteriosus (PDA) has been infrequently documented in older children. This study aims to present our experience with ductal spasms observed during transcatheter occlusion procedures for PDA.

Material and Methods: A retrospective analysis was conducted on transcatheter PDA occlusions (n=544) performed at our clinic between 2010 and 2022.

Results: Eleven patients (2%) were identified to have experienced ductal spasms during the transcatheter PDA occlusion procedure. Nine patients were born prematurely between 25 and 35 weeks of gestation, while two were born at full term. The median age at the time of the procedure was 17 months (range: 10-87 months). Eight patients received supplemental oxygen during the procedure. Device embolization occurred in two patients; however, the embolized devices were successfully retrieved, and larger devices were subsequently implanted. Closure of the PDAs was achieved using Amplatzer Vascular Plug-2 (n=10) and Amplatzer Duct Occluder-2 (n=1).

Discussion: Ductal spasm primarily manifests in preterm infants, even during infancy, particularly those receiving oxygen therapy. It is imperative to minimize the use of oxygen during transcatheter PDA occlusion procedures. Preoperative echocardiographic measurements consistently demonstrate superior reliability compared to angiographic measurements. Therefore, they should be given due consideration when assessing and selecting an appropriate device. Double-disk devices may be preferable for closing the ductus in patients at risk of PDA spasm or with a history of PDA spasms.

Keywords

Patent Ductus Arteriosus, Prematurity, Ductal Spasm, Transcatheter Closure

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Introduction

Patent ductus arteriosus (PDA) is one of the most prevalent congenital heart diseases observed across all age groups. In most full-term infants, the ductus arteriosus closes functionally within a few hours following birth, and anatomical closure typically occurs within 2 to 8 weeks. Nevertheless, the persistence of an open ductus beyond 72 hours of postnatal age, known as a persistent ductus arteriosus, is frequently encountered in nearly 50% of premature infants [1]. However, the incidence of delayed closure is comparatively less frequent in neonates born at full term. Intermittent spasms and subsequent patency of ductus rarely occur in premature cases following pharmacological ductal closure. Such a phenomenon has been described in term neonates; however, it is extremely rare in older children and has been presented in a few case reports in the literature [2, 3, 4]. However, transcatheter occlusion, an emerging standard procedure, can be complicated by rare ductal spasm during cardiac catheterization, causing procedural failure, underestimation of duct and device size, and potential embolization [1, 3].

In this report, we present our experience concerning the occurrence of ductal spasms during transcatheter occlusion of PDA, where the presence of spasm complicated the procedure and influenced the selection of an appropriate device for these patients.

Material and Methods

A retrospective analysis was conducted, encompassing a total of 544 cases of transcatheter occlusion of PDA performed at our clinic between 2010 and 2022. The study was planned in accordance with the Declaration of Helsinki after obtaining the required approval from the local ethics committee (no: 2022-67, expiry date: 28.11.2022).

Device occlusion was conducted in patients with significant left-to-right shunting via PDA, which results in echocardiographic parameters of left atrial and/or left ventricular volume overload. Before the procedure, the interventional cardiologist conducted comprehensive physical examinations and echocardiographic assessments on the same day. All patients exhibited continuous heart murmurs consistent with a PDA, accompanied by echocardiographic evidence of left-heart volume overload.

Cardiac catheterization procedures were carried out under general anesthesia while patients were ventilated with a laryngeal mask. Vascular access was obtained using the modified Seldinger technique. Baseline hemodynamic measurements, including mean pulmonary artery and aortic pressures, were recorded prior to the initiation of the procedure. Biplane aortic angiograms were subsequently performed to evaluate the characteristics of the PDA, encompassing measurements of aortic and pulmonary side diameters, the narrowest segment, and length. Based on these observations, an appropriate device was selected in accordance with established guidelines [5]. Antegrade delivery from the venous circulation was the preferred method for device deployment, whereas retrograde deployment was infrequently employed. Subsequent to device deployment, angiography in the descending aorta through the delivery catheter was conducted to confirm the final positioning of the device relative to the pulmonary arteries. If the device was deemed to be satisfactorily positioned, it was released accordingly.

The presence of significant ductal spasms was defined based on the following observations:

1. Echocardiographic examination revealed a notably larger PDA prior to the angiographic procedure.
2. Initial aortic angiogram indicating minimal flow through the PDA.
3. Relief of the spasm was observed in angiography that was performed 15-20 minutes after the initiation of aorta-to-pulmonary artery flow.

For cases exhibiting ductal spasm, a comprehensive collection of data was recorded, including gestational age, birth weight, age at the time of the procedure, physical examination findings, echocardiographic findings before and during catheterization, angiographic data, details regarding the type and diameter of the PDA after spasm relief, device specifications, and recent echocardiographic follow-up information.

Statistics

Statistical analysis was conducted employing SPSS 25 software (SPSS, Chicago, IL, USA). Categorical variables were presented as total counts, mean values accompanied by the standard deviation (SD) in cases where the data followed a normal distribution or as medians with ranges (minimum to maximum) in instances where the data did not exhibit a normal distribution.

Ethical Approval

Ethics Committee approval for the study was obtained.

Informed consent was obtained from the patient's parents.

Results

A total of eleven patients (2%) exhibiting ductal spasms during transcatheter occlusion of PDA were identified. Among them, nine patients were born within the gestational age range of 25 to 35 weeks, while the remaining two were born at full term (Figure 1). The median age at the time of the procedure for patients experiencing ductal spasms was 17 months, ranging from 10 to 87 months. Comprehensive demographic and clinical data of these patients are summarized in Table 1.

Echocardiographic assessments revealed minimum ductus diameters ranging from 3 to 6.4 mm. Notably, in 10 out of 11 patients, the occurrence of spasm preceded the passage of the catheter through the PDA. Eight of the patients who experienced ductal spasm were receiving oxygen during the procedure. Subsequently, upon re-auscultation, a reduction in murmur intensity was observed concomitant with the onset of ductal spasm in all patients. Following the relief of the spasm, minimal PDA diameters ranged from 2.8 to 5.6 mm, with a median value of 3.5 mm. Deployment of the devices took place anterogradely from the venous circulation in nine cases, while the retrograde route was employed in the remaining two instances. Detailed cardiac catheterization findings are presented in Table 2.

During percutaneous occlusion procedures for PDA conducted between 2010 and 2016, all patients underwent oxygen ventilation administered by the anesthesiologist. Within this specified period, we observed the occurrence of ductal spasms in seven patients, all of whom were premature infants. During the occurrence of ductal spasm, a remarkable decrease

in murmur and precordial thrill was observed, coinciding with a concomitant reduction in the flow of the PDA into the pulmonary artery as evidenced by echocardiographic evaluations. Subsequently, upon realizing that the patients were receiving oxygen, the administration of supplemental oxygen was promptly discontinued. The continuous murmur reappeared after a waiting period of 15 to 20 minutes. Notably, following the relaxation of the PDA, all devices were successfully deployed without any residual shunting. For six patients (except patient number six), ductal spasms occurred before the catheter crossed the ductus.

Our prior experience with ductal spasms was limited before the year 2016. In two patients, device embolization occurred. Specifically, in patient 6, successful deployment of a 5.5 mm Nit-Occlud® PDA-R device (PFM Medical, Cologne, Germany) resulted in minimal residual flow. However, the subsequent day witnessed the embolization of the device to the descending aorta. The embolized device was effectively retrieved using an Amplatz Gooseneck snare (Microvena, St. Paul, MN, USA), and the duct was subsequently occluded using an 8 mm Amplatzer Vascular Plug 2 (St. Jude Medical, Inc., St. Paul, MN, USA).

In the case of the 7th patient, the ductus was successfully occluded using an 8 mm AVP-2 device. However, the device embolized to the right pulmonary artery on the following day. The embolized device was promptly extracted, and closure of the PDA was subsequently accomplished by employing a 10 mm AVP-2 device (Figure 2). In these two cases, during the initial procedure, we observed that the angiographically measured diameter of the duct was smaller than the expected size. Consequently, a small-sized single-disc device was employed for patient 6, while a small double-disc device was utilized for patient 7. Upon retrieving the embolized devices the subsequent day, a double-disc device was implemented for duct occlusion in both patients. After this unpleasant yet instructive experience, ductal occlusion procedures were subsequently guided not only by small angiographic measurements but also by echocardiographic measurements or angiographically relieved ductal measurements, and then double-disc devices were used.

Following these distressing events, we provided guidance to the anesthesiologist to refrain from administering oxygen to patients scheduled for PDA occlusion prior to the procedure. In patients who underwent ductal occlusion after 2016, the anesthesiologist diligently focused on minimizing the inhaled oxygen fraction to 21% whenever feasible. However, despite these precautions, an additional four cases of ductal spasms were encountered. The first case was a seven-year-old female patient (patient 8), who was born prematurely at 30 gestational weeks weighing 1480 grams. She was ventilated with 21% FiO2 during the procedure. The second case was a three-year-old girl (patient 9). She was born full term at the 38th gestational week, weighing 2300 grams, but required supplemental oxygen during the procedure due to excessive secretion. The penultimate patient (patient 10) was a one-year-old male with a history denoting full-term delivery (40th gw, 3500 g). This patient did not necessitate supplemental oxygen, though he experienced emesis during the induction of anesthesia despite maintaining normotensive arterial pressure. The last patient (patient 11) was a one-year-old female infant, born prematurely at 29 gestational weeks and weighing 1440 grams, and she did not require supplemental oxygen support during the procedure.

Over the years, our awareness of the disease was heightened, and none of the patients with ductal spasm were seen after 2018, indicating an enhancement in our approach. Concerning follow-up, no severe complications occurred in any patient. All patients were asymptomatic and had normal left-heart volumes without a residual ductus arteriosus or an obstruction to the branch pulmonary artery and aortic flows.

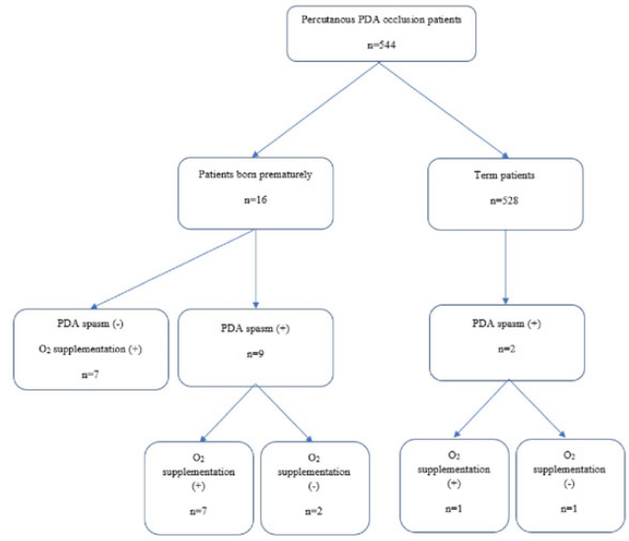

Figure 1. Characteristics of the patients who underwent transcatheter PDA occlusion. PDA, patent ductus arteriosus.

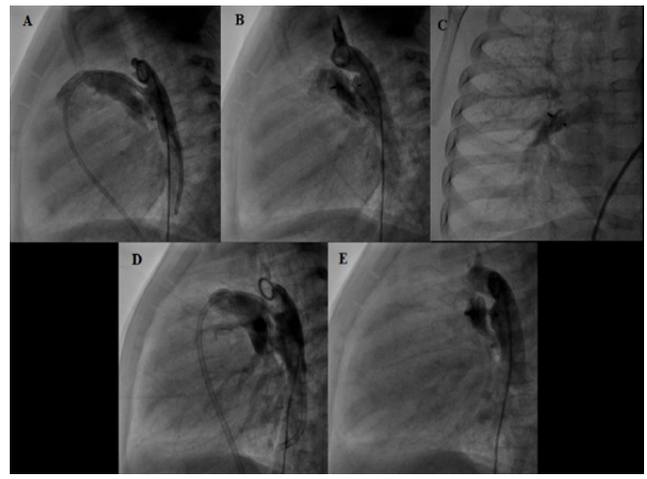

Figure 2. Angiographic images of patient 7 who experienced ductal spasm and embolization of the device. A. Initial aortic lateral angiogram demonstrating ductal spasm. B. Angiogram showing 8 mm AVP-2 device, which was inserted with no residual flow. C: AP Fluoroscopic image demonstrating the embolized device in the right pulmonary artery. D. Lateral angiogram demonstrating the relieved PDA flow. E. Lateral angiogram demonstrating the placement of a 10 mm AVP-2 device in the relieved PDA. AP, anterior-posterior; AVP-2, Amplatzer vascular plug 2; PDA, patent ductus arteriosus.

Table 1. Diagnostic and Demographic Findings.

Patient	Gender	Birth weight (g)	Gestational age (weeks)	Age at the procedure (years)	Weight at the procedure (kg)	Echocardiography	
						PDA Minimal luminal diameter (mm)	Left heart volume overload
1	F	1600	30	1.00	8.5	4.8	Yes
2	M	2100	34	3.08	17.2	3.5	Yes
3	F	1240	28	1.42	9.9	4.5	Yes
4	F	800	25	3.33	14.6	3.5	Yes
5	M	1280	28	1.42	10.3	3	Yes
6	M	2320	35	1.42	9	4,5	Yes
7	M	1310	29	0.83	6.5	6.4	Yes
8	F	1480	30	7.25	35	4.5	Yes
9	F	3200	38	2.92	17.5	4	Yes
10	M	3500	40	1.25	10	3.5	Yes
11	F	1440	29	1.25	11	3	Yes

PDA; patent ductus arteriosus

Table 2. Catheterization Data.

Patient	MAP (mmHg)	Type	Diameter (mm) (aortic end)	Diameter (mm) (pulmonic end)	Length (mm)	Oxygen supplement	Route of PDA closure	Device
1	30	C	7	4.2	19.7	Yes	Antegrade	8 mm AVP-2
2	23	C	6	3.5	18.5	Yes	Antegrade	8 mm AVP-2
3	17	C	3.7	5.6	18	Yes	Antegrade	10 mm AVP-2
4	28	C	5.4	3.5	6.7	Yes	Retrograde	5/4 ADO-2
5	21	C	5.6	3.3	12.8	Yes	Retrograde	8 mm AVP-2
6	17	C	10.9	4	18	Yes	Antegrade	8 mm AVP-2
7	24	C	7.4	3.5	11.7	Yes	Antegrade	10 mm AVP-2
8	23	C	7.5	4.5	13	No	Antegrade	10 mm AVP-2
9	34	C	11.5	4.2	10.3	Yes	Antegrade	8 mm AVP-2
10	15	E	8	3.5	7	No	Antegrade	8 mm AVP-2
11	18	C	3	2.8	6	No	Antegrade	5/4 ADO-2

ADO-2; Amplatzer duct occluder-2, AVP-2; Amplatzer vascular plug-2, MAP; mean arterial pressure, PDA; patent ductus arteriosus

Discussion

Ductal spasm is a condition that occurs during transcatheter occlusion and may be an unpredictable cause of procedural failure. Successful percutaneous closure of the patent ductus arteriosus (PDA) relies heavily on an accurate assessment of the ductal morphology, which includes a detailed understanding of its length, the narrowest segment, and the overall shape and configuration. The importance of a judicious selection of an appropriate occlusion device for a successful procedure cannot be overstated.

The onset of ductal spasm, whether spontaneous or induced by manipulation of the duct, presents a challenging variable that might lead to an underestimation of the ductus arteriosus dimensions. This miscalculation may lead to the selection of an inappropriate occlusion device and the unintentional embolization of devices, as seen in prior studies [1, 3]. The sporadic spasm of the ductus beyond neonatal stages was first observed through auscultatory changes and subsequently confirmed via echocardiography and angiography [3, 6, 7, 8]. Even though the precise mechanisms that trigger the vascular reactivity of the ductus arteriosus are yet to be unraveled entirely, a number of physiological, hemodynamic, and pharmacological factors have been proposed as possible contributors to the patency or constriction of the ductus arteriosus. The presence of smooth muscle cells at the pulmonary artery end of the ductus suggests the potential site of narrowing in affected cases [5, 8, 9]. Specific triggers, such as catecholamines, have been shown to potentially induce ductal constriction, particularly in children with a history of low birth weight and a potentially lower gestational age [10]. Moreover, agents like oxygen, bradykinin, histamine, 5-hydroxytryptamine, and acetylcholine have been found to influence ductal constriction according to numerous studies [3, 5, 7, 9, 10, 11, 12].

While the ductus arteriosus reactivity in older children is considered an uncommon phenomenon and has been sparsely documented in the literature, it is known to occur [3, 6, 7, 10]. However, some professionals have doubts about the likelihood of duct diameter changes occurring without any direct or indirect manipulation of the ductus arteriosus [6]. Notable instances include Cokkinos et al.'s report of the intermittent disappearance of a PDA murmur in a ten-year-old patient [2], as well as a documented case from Germany revealing the reactivity of a patent arterial duct in a one-year-old infant during a routine echocardiographic study [6]. In our study, similar to other reports, ductal spasm occurred without catheter manipulation in most of the patients (n=10, 91%). Nonetheless, several case reports present a different viewpoint. In these

reported cases, catheter-induced vasospasm was considered as a possible causative factor [3, 7]. In our series, we encountered a case where ductal reactivity likely occurred subsequent to direct manipulation of the duct.

Prematurity appears to be the prevailing associated anomaly in the vast majority of previously reported cases [3, 10, 11]. For instance, Batlivala et al., in their research, identified seven cases of ductal spasms out of 331 (2.1%), all of whom were prematurely born. The median age of these patients was 12 months, with a median gestational age of 28 weeks [10]. In our own series spanning 13 years and covering 544 ductal occlusions, we encountered 11 cases (2%) of ductal spasms. Among the 16 patients who underwent transcatheter occlusion for PDA in our research, nine had a history of preterm delivery and later developed ductal spasms. Conversely, the other two infants who experienced a ductal spasm were born after completing 37 weeks of gestation. In our patient group, the median age at the time of intervention was 17 months.

Studies have indicated that the ductus arteriosus musculature demonstrates sensitivity to oxygen, a potent constrictor for the fetal PDA [10, 12]. In the report by Phyu et al., they shared their experiences about ductal spasms that occurred during transcatheter occlusion in two children without any catheter manipulation and stated that the cause of spasms could be oxygen or catecholamines [12]. Until 2016, we routinely administered oxygen during transcatheter ductal occlusion procedures. However, frequent occurrences of ductal spasms led us to decrease inhaled oxygen levels, aiming for a FiO2 of 0.21. Of the eight patients who experienced ductal spasms during our study, seven were preterm infants, and one was a full-term infant, all initially receiving oxygen supplementation. These findings suggested that oxygen may play a role in the development of ductal spasms.

One of the risks of PDA spasm is device embolization due to inappropriate device selection, as stated in the literature [1, 3, 9, 12]. Among our patient cohort, two experienced embolization of the occlusion device due to undersizing. The remaining nine patients received relatively large, double-disc ductal occlusion devices. We advise a minimum 15-minute waiting period if a ductal spasm transpired prior to the catheter crossing the ductus for spasm relief and assessment of any underlying causes. Ensuring appropriate occlusion device selection necessitates careful echocardiographic measurements and proactive steps to prevent device undersizing.

Tomita et al. explored the effect of catecholamines on the ductus arteriosus, proposing a hypothesis that the sympathetic response initiated during crying might contribute to the temporary occlusion of the PDA. Within this investigation, the intravenous administration of epinephrine, norepinephrine, and dobutamine substantially constricted the ductus arteriosus within a span of 10 to 15 minutes post-injection, demonstrating a discernible contraction at the pulmonary artery end of the ductus arteriosus [11]. A noteworthy case in our study involved a full-term infant who underwent the procedure with a FiO2 of 0.21. Following anesthesia induction, the patient experienced vomiting. There was a reduction in the ductal diameter from an initial echocardiographic measurement of 3.5 mm to 2 mm during the procedure, prompting contemplation of the potential impact of catecholamines on ductal constriction.

All of our cases presented with murmurs indicative of PDA during pre-procedural auscultation. However, the absence of a ductal murmur during a spasm underlines the importance of a comprehensive examination to avert misinterpretation based solely on catheterization data. We strongly advocate routine patient evaluation prior to procedures to ensure accurate diagnostic information.

Our findings indicate that ductal spasms may initiate spontaneously or in response to oxygen supplementation, adrenergic stimuli (such as vomiting), or ductal manipulation via catheter or wire. This occurrence seems more prevalent among oxygen-receiving preterm infants, yet it can also arise in term infants. Despite historical evidence highlighting the primary manifestation of ductal spasm in neonates, it may also occur in older age groups. Thus, clinicians must consider the potential for ductal spasm when disparities emerge between clinical examination, echocardiography findings, and catheter angiography results.

Study limitations

This study has certain limitations to consider. As an observational investigation, it focused on a relatively small cohort of patients experiencing ductal spasm, with all data collected retrospectively from a single medical center. This may influence the overall generalizability and applicability of the findings.

Conclusions

Ductal spasm predominantly manifests in preterm infants, even during the early stages of infancy, particularly in those receiving oxygen therapy. It is strongly recommended to minimize the use of oxygen during transcatheter PDA occlusion procedures. Preoperative echocardiographic measurements consistently exhibit greater reliability compared to angiographic assessments. Hence, these measurements should be considered when determining the appropriate device selection. Double-disk devices can be preferred to close the ductus in patients with ductal spasm or risk of ductal spasm.

Scientific Responsibility Statement

The authors declare that they are responsible for the article's scientific content including study design, data collection, analysis and interpretation, writing, some of the main line, or all of the preparation and scientific review of the contents and approval of the final version of the article.

Animal and human rights statement

All procedures performed in this study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. No animal or human studies were carried out by the authors for this article.

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Conflict of interest

The authors declare no conflict of interest.

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